DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/31/2009 has been entered.

Response to Arguments

Applicants present arguments by way of Declarations by Vandevelde and Volk. In particular, Vandevelde is of the opinion that the use of AWD 131-138 for the treatment of idiopathic epilepsy in dogs was not obvious at the time the subject patent application was filed. Vandevelde argues that the animal models of electrical induction seizures, chemical induction of seizures and audiogenic seizure are not models that provide a suggestion that a compound is used as an anticonvulsant in idiopathic epilepsy in dogs. It is discussed that drugs with rapid metabolism and rapid elimination are not successful anticonvulsants in man because idiopathic seizures can occur at any time. Vandevelde discusses that drugs which are useful for treatment of human epilepsy are in most cases not useful for the treatment of canine epilepsy.

Vandevelde points to a paper by Loscher et al. in which a review of available anticonvulsants tested that are useful in humans were found not to be useful in dogs in idiopathic epilepsy. Vandevelde also points to a paper by Rostock in which it is argued

that data from experimental animal models are of limited relevance for the treatment of canine epilepsy. Vandevelde discusses that canines metabolize chemicals very quickly, resulting in short half lives and low plasma levels and experimental animal data or data generated in human patients can be extrapolated to epileptic dogs for this reason.

In response to the above arguments concerning the Loscher reference, it is noted that the reference discusses that previous studies suggest that epilepsy in dogs closely approximates the disease in man (see first paragraph of Discussion). Further, Loscher concludes that the data of that particular article supplied by Applicants indicate that the epileptic dog is indeed a suitable model of human epilepsy. Further, Loscher found parallels between some of the antiepileptics tested, for instance, the efficacy of primidone in dogs corresponds with that in humans (see fourth paragraph in Discussion). This refutes the argument that definitions of human epilepsy cannot be extrapolated to dogs because the Loscher article presented by Applicants shows a clear parallel with a lot of anticonvulsants available at that time.

Regarding the arguments concerning the Rostock reference supplied by Applicants that data shows that data from experimental animals are of limited relevance in the treatment of canine epilepsy, it is unclear how this reference makes this point. The reference focuses on one particular drug in comparison to other known anti-epileptics in rodents. It is requested that further explanation be made to show that this reference is relevant to the conclusion that data from experimental animals are of limited relevance in the treatment of canine epilepsy.

The Declaration by Volk makes similar arguments. In particular, Volk argues that treatment options for canine idiopathic epilepsy are very limited to this day. Volk discusses the metabolism of drugs by dogs as being very different from humans and that a compound that is active in humans is not predictive of treatment of canine epilepsy. Volk is of the opinion that it would not be obvious to administer AWD 131-138 in the treatment of idiopathic epilepsy in canines. Supplied with the Volk Declaration is a paper by Yarrington in which it is taught vigabatrin is used as treatment for some types of epilepsy in animals but causes intramyelinic edema. Volk states that the reference teaches that administration to dogs resulted in unexpected toxic effects presenting as neuropathology. Further, Volk points to an article by Schicht et al. and argues that oxcarbazepine is used for human epilepsy but was not effective in the treatment of epileptic dogs.

While the above arguments and papers are fully appreciated, it is clear from the references that two particular drugs (vigabatrin and oxcarbazepine) are effective in treating human epilepsy but are not effective in treating dogs. This phenomenon is quite frequent in the testing of clinically relevant drugs. There are many drugs that are tested in preclinical situations that are effective in the chosen animal model, but do not translate to efficacy in humans.

Further, the above Declarations and arguments were addressed accordingly; however, it should be noted that the rejections made were not based on AWD 131-138 being effective in humans and therefore making the presumption that it will be effective in dogs. The references used in the rejection were made to teach that AWD 131-138

was tested in animal models of idiopathic epilepsy (Bialer) and two references were utilized to define the different types of epilepsy and to conclude that Bialer teaches idiopathic epilepsy. The Declaration by Vandevelde points to several tests in the Bialer reference and argued that the tests were not idiopathic seizure activity but were induced. It is noted that Bialer teaches animal models that include WAG rats which are rat models of genetic epilepsy and for absence seizures, which is a form of idiopathic epilepsy. Animal model testing not only extrapolates to humans but to other animals as well. Further, there is evidence as discussed in previous responses and above, that human and canine epilepsy have similar etiologies and can be defined the same.

Accordingly, the rejection is maintained and given below for Applicants convenience.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-15 and 19 rejected under 35 U.S.C. 103(a) as being unpatentable over Bialer et al. (J Epilepsy Research (Jan 2001) 43, pgs. 11-58) in view of Ross et al. (Neurosci Biobehav Rev, 24 (2000) 639-653) and French (Am J Managed Care, Vol. 7, No. 7, 2001).

Bialer et al. teach that AWD 131-138 treats audiogenic clonic seizures and absence epilepsy in genetic models of epilepsy (meeting the limitation of claim 12; pg. 12, Section 2.1.1.1). Because it is taught that AWD 131-138 has anticonvulsant activities in animal models of epilepsy, it is obviously taught that AWD 131-138 would effectively treat epilepsy regardless of when it was diagnosed (meeting the limitation of claim 19). Though Bialer et al. does not teach the treatment of dogs with AWD 131-138 in the AGS model or in absence epilepsy, the treatment of dogs is taught in other models. Therefore, there would be a reasonable expectation of success that AWD 131-138 would be an effective treatment for idiopathic epilepsies.

Bialer et al. does not specifically state that the forms of epilepsies are idiopathic.

Ross et al. teach that AGS is a form of epilepsy associated with generalized seizure displayed by clonic or tonic-clonic seizure activity (see first paragraph of Introduction).

French teaches that clonic or tonic-clonic seizure activity is a form of idiopathic epilepsy (see Role of New AEDs on page S209).

Because Ross et al. and French teach that AGS is a form of idiopathic epilepsy, it would be obvious to a person of ordinary skill in the art at the time of the invention that Bialer et al. is teaching the treatment of different forms of idiopathic epilepsy with AWD 131-138. Though Bialer et al. does not teach the treatment of dogs with AWD 131-138 in the AGS epilepsy model or in absence epilepsy animals, the treatment of dogs is taught in other models. Therefore, there would be a reasonable expectation of success that AWD 131-138 would be an effective treatment for idiopathic epilepsies. One would

be motivated to treat idiopathic epilepsy with AWD 131-138 with a reasonable expectation of success because it is taught that AWD 131-138 is effective in treating AGS and absence epilepsy, which is a form of idiopathic epilepsy.

It is noted that the claim limitation of "…said idiopathic epilepsy being characterized by excessive transient paroxysmal neuronal discharge in the cerebral cortex of said dog, when no underlying cause can be found via clinical and pathological examination…" refers to the mechanism of action of the idiopathic epilepsy. If it is determined that the treatment will treat idiopathic epilepsy, then it will obviously treat idiopathic epilepsy, regardless of how it is characterized.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bialer et al. (J Epilepsy Research (2001) 43, pgs. 11-58) in view of Ross et al. (Neurosci Biobehav Rev, 24 (2000) 639-653) and French (Am J Managed Care, Vol. 7, No. 7, 2001) as applied to claims 12-15 and 19 above, in view of Thomas (Veterinary Clinics of North America Small Animal Practice (2000), 30, pgs. 183-206).

Bialer et al. teach that AWD 131-138 treats idiopathic epilepsy in dog seizure models as described in the above rejection.

Bialer et al. does not teach the co-administration of another active ingredient.

Thomas et al. teach that Phenobarbital is the initial choice of treatment for idiopathic epilepsy in dogs (meeting the limitations of claims 16-17; pg. 191, Choice of Treatment).

It would be obvious to one having ordinary skill in the art at the time of the invention that AWD 131-138 would be successful in treating idiopathic epilepsy in dogs by the teachings of Bialer et al., which teach that AWD 131-138 is effective in treating animal-models of idiopathic epilepsy. Furthermore, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, 1072 (CCPA 1980). Therefore, it would be obvious to co-administer another active ingredient such as Phenobarbital because it is useful in the treatment of idiopathic epilepsies as taught by Thomas et al. One would be motivated to administer the combined treatment with a reasonable expectation of success because both AWD 131-138 and Phenobarbital are taught to effectively treat idiopathic epilepsy.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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